Preface: Extracellular vesicles in the tumour microenvironment

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Cancer is a devastating disease that touches the lives of millions of people around the world. After many years of work by thousands of scientists and clinicians around the globe the overall survival of patients who acquire certain types of cancer has been dramatically improved. However, the overall survival rates for some forms of cancer remain stubbornly low. It is therefore imperative to devise novel avenues of research from which to derive new opportunities for drug development and identification of new tools for early diagnosis and disease monitoring.

One such emerging area of intensive research is the concept of the tumour microenvironment. Cancer cells do not grow as a homogenous mass, existing in isolation from other cell types, but rather in collaboration with other cells in the environment of the tumour. These stromal cells, which under normal conditions support the function of healthy tissues, surround and perfuse the tumour mass and interact with cancer cells. This communication in the tumour microenvironment often leads to the corruption of the stromal cells, allowing them to inappropriately stimulate and support the growth of the tumour. Understanding the signalling mechanisms between the different cells of the tumour microenvironment holds promise as the key to developing new therapeutics that could block the cancer's support mechanism.

Extracellular vesicles (EVs) are small lipid-bound vesicles released by cells into the extracellular space. Initially thought of as a biological curiosity, they are now known to be important messengers mediating the dialogue between cells. The cargo they carry can either be internalised and utilised by recipient cells or interact with receptors at the plasma membrane leading to intracellular signalling. One cell can therefore affect the phenotype of another cell via the transfer of EVs with specific types of cargo such as RNA or protein. EVs have been shown to have a number of roles, including in regulating the immune system, angiogenesis and stress responses. Importantly, their dysregulation can have pathological effects and their abnormal function has been implicated in cancer.

The combination of these two novel fields has led researchers to study the role of EVs in the tumour microenvironment. This convergence of disciplines has led to exciting new insight into the way in which tumours are affected by EV-mediated communication between cancer and stromal cells. Like any new field with promise it needs to be nurtured and supported. For this reason the Royal Society held a Science Meeting in January 2017 entitled "Extracellular Vesicles and the Tumour Microenvironment". This exciting meeting was well attended and led to this special edition of the

Philosophical Transactions B. In this special edition we start with a more detailed introduction to the topic and the meeting. The rest of the special edition, which includes reviews, opinion pieces and research articles, describes various aspects of EV biology in the tumour microenvironment. The review articles and opinion pieces cover a range of aspects, including EV heterogeneity, the role of lipids and EVs in tumour progression, EVs in cell senescence, cell death and immune function, and the way in which miRNAs carried by EVs can acts as ligands to trigger the activation of receptor proteins. The research articles describe how EVs released by ovarian cancer cells treated with chemotherapy can affect other cells in the vicinity leading to tumour progression, and how EVs released by glioblastoma cells can alter human astrocytes leading them to be pro-tumorigenic.

The exciting field of EVs in the tumour microenvironment is growing rapidly. Greater understanding could lead to novel therapeutics to tackle cancer, and new tools to aid diagnosis and prognosis. We hope that readers will enjoy this special edition of Philosophical Transactions B, which sheds light on this expanding field.